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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/775,967

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Andrei P. Guzaev

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06/11/2003

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EXAMINER

LEWIS, PATRICK T

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 06/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/775,967

Applicant(s)

GUZAEV ET AL.

Examiner

Patrick T. Lewis

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-105 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 21, 47-52, 56-60, 66, 81-85, 92-98, 101, 102 and 104 is/are rejected.
- 7) ☒ Claim(s) 11-15, 36-40, 99, 100 and 103 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Continuation of Disposition of Claims: Claims withdrawn from consideration are 7-10,16-20,22-35,41-46,53-55,61-65,67-80,86-91 and 105.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of the species wherein  $D^+$  is protonated aromatic heterocyclic amine and  $E^-$  is tetrazolide anion in Paper No. 6 dated December 24, 2002 is acknowledged. The traversal is on the ground(s) that the generic claim is searchable without difficulty. This is not found persuasive because the examiner is responsible for not only searching the art area but also the specific nature of the subject matter applicant regards as their invention. Applicant's opinion that the claims as originally filed would not impose a serious burden upon the examiner in charge of this application is duly noted. The examiner has established that the species are indeed patentably distinct and the examiner has determined an examination of all the claims in this application would indeed impose a undue burden.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 7-10, 16-20, 22-35, 41-46, 53-55, 61-65, 67-80, 86-91, and 105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6 dated December 24, 2002.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1623

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 48-52, 56-60, 66, 81-85, 92-95, and 104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 48, the variable  $R^2$  is not clearly defined. " $R^2$  is a 2'-substituent" does not apprise one of ordinary skill in the art of the metes and bounds of the invention. Claim 48 also recites the variables  $R^4$  and  $R^5$ . Variables  $R^4$  and  $R^5$  are not depicted in the structural formula. This ambiguity renders the claim indefinite as one of ordinary skill would not be able to determine the scope of the claimed invention.

### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Art Unit: 1623

7. Claims 1-6, 21, 47-52, 66, 92-93, 96-97, and 104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caruthers et al. Proceedings of the 2<sup>nd</sup> International Symposium on Phosphorous Chemistry Directed Towards Biology (1987), pages 3-21 (Caruthers) in combination with Beaueage et al. Tetrahedron (1992), Vol. 48, pages 2223-2311 (Beaueage).

Claims 1-6, 21, and 47 are drawn to a method comprising reacting a nucleoside phosphoramidite with a support bound oligomer in the presence of a neutralizing agent, wherein said neutralizing agent is an aliphatic amine, an aliphatic heterocyclic amine, an aromatic amine, an aromatic heterocyclic amine a guanidine, or a salt of formula  $D^+E^-$ . Claims 48-52, 66, 92-93, and 104 are drawn to a method of forming an internucleoside linkage in the presence of a neutralizing agent, wherein said neutralizing agent is an aliphatic amine, an aliphatic heterocyclic amine, an aromatic amine, an aromatic heterocyclic amine a guanidine, or a salt of formula  $D^+E^-$ . Claims 96-97 are drawn to a method comprising the steps of: a) providing a solid support having a 5'-O-protected phosphorous-linked oligomer bound thereto; b) deprotecting the 5'-hydroxyl of the protected oligomer; c) optionally washing the deprotected phosphorous-linked oligomer on the solid support; d) contacting the support bound oligomer with a solution comprising a 5'-protected nucleoside phosphoramidite and a neutralizing agent; and e) oxidizing or sulfurizing the phosphite triester linkage.

Caruthers teaches the synthesis of oligonucleotides using the phosphoramidite method corresponding to the instantly claimed method. Using the procedure outlined in Table 1 (page 6), RNA was synthesized manually. Support bound nucleoside (3a-d)

Art Unit: 1623

was first converted to **5a-d** by treatment with 0.3% DCA to remove the dimethoxytrityl group. After washing with dichloromethane and acetonitrile, the appropriate nucleoside phosphoramidite (**4a**, **4b**, **4c**, or **4d**) and tetrazole were added to the support. Condensations were allowed to proceed for 15 minutes. Following an aqueous, hydrolytic wash the final two steps oxidation with  $I_2$  and capping with benzoic anhydride.

Caruthers differs from the instantly claimed invention in that Caruthers does not teach the use of a neutralizing agent of  $D^+E^-$ ; however, the use of a neutralizing agent of the formula  $D^+E^-$  as a suitable replacement for tetrazole would have been obvious to one of ordinary skill in the art when the teachings of Beaueage are considered.

Beaueage teaches the use of either 1H-tetrazole or its N,N-diisopropylammonium salt for the facile preparation of deoxyribonucleoside phosphoramidites from the selective activation of phosphoradiamidites. The selection of a known material based on its suitability for its intended use is prima facie obvious as Beaueage teaches the use of either 1H-tetrazole or its N,N-diisopropylammonium salt for the selective activation of phosphoradiamidites.

8. Claims 98 and 101-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caruthers et al. Proceedings of the 2<sup>nd</sup> International Symposium on Phosphorous Chemistry Directed Towards Biology (1987), pages 3-21 (Caruthers) in combination with Beaueage et al. Tetrahedron (1992), Vol. 48, pages 2223-2311 (Beaueage):

Claims 98 and 101-102 are drawn to a composition comprising a 5'protected nucleoside phosphoramidite and a salt of formula  $D^+E^-$ .

Art Unit: 1623

Caruthers teaches support bound nucleoside (**3a-d**) which are first converted to **5a-d** by treatment with 0.3% DCA to remove the dimethoxytrityl group. After washing with dichloromethane and acetonitrile, the appropriate nucleoside phosphoramidite (**4a**, **4b**, **4c**, or **4d**) and tetrazole [neutralizing agent] were added to the support.

Caruthers differs from the instantly claimed invention in that Caruthers does not teach the use of a neutralizing agent of formula  $D^+E^-$ ; however, the use of a neutralizing agent of the formula  $D^+E^-$  as a suitable replacement for tetrazole would have been obvious to one of ordinary skill in the art when the teachings of Beaueage are considered.

Beaueage teaches the use of either 1H-tetrazole or its N,N-diisopropylammonium salt for the facile preparation of deoxyribonucleoside phosphoramidites from the selective activation of phosphoradiamidites. The selection of a known material based on its suitability for its intended use is prima facie obvious as Beaueage teaches the use of either 1H-tetrazole or its N,N-diisopropylammonium salt for the selective activation of phosphoradiamidites.

### ***Conclusion***

9. Claims 1-105 are pending. Claims 7-10, 16-20, 22-35, 41-46, 53-55, 61-65, 67-80, 86-91, and 105 are drawn to a nonelected invention. Claims 1-6, 21, 47-52, 56-60, 66, 81-85, 92-98, 101-102, and 104 are rejected. Claims 11-15, 36-40, 99-100, and 103 objected to as being dependent upon a rejected base claim, but would be allowable if



Art Unit: 1623

rewritten in independent form including all of the limitations of the base claim and any intervening claims.

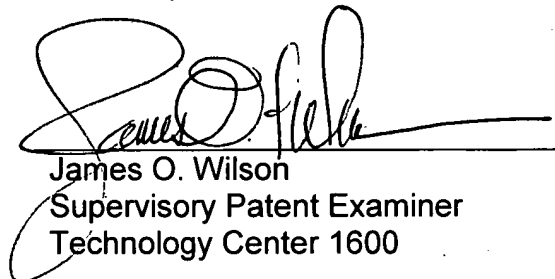
### ***Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 10:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patrick T. Lewis, PhD  
Examiner  
Art Unit 1623



James O. Wilson  
Supervisory Patent Examiner  
Technology Center 1600

ptl  
June 10, 2003